RECAST-3

SITE INVESTIGATOR MEETING

Remote Ischaemic Conditioning After Stroke 3 (RECAST-3)

A multicentre randomised controlled trial

06/11/2024

recast-3@nottingham.ac.uk

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REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

AGENDA

1. Trial PICO
2. Sites and recruitment update
3. Trial updates and reminders
    i. Upcoming amendment
    ii. Emergency contact numbers
    iii. Co-enrolment
    iv. Overseas patients
    v. Patients due for repatriation
    vi. Site-to-site transfers
    vii. Entry of missing data
    viii. Data corrections
    ix. Device checks
    x. Ward staff training
4. Questions

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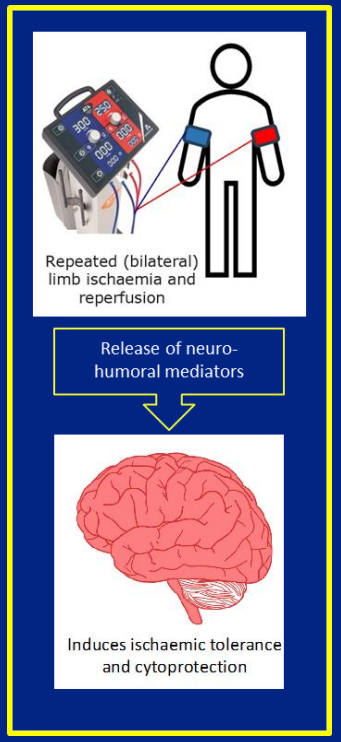
TRIAL PICO

- **Setting:** 60 UK NHS Trusts
- **Population:** 1,300 patients with acute (≤24 hours) ischaemic stroke
- **Intervention:** 4 cycles of intermittent bilateral limb ischaemia - alternating 5 minutes inflation (+20 mmHg above systolic BP) followed by 5 minutes deflation of bilateral upper arm blood pressure cuffs. Twice daily (am/pm) for 14 days/28 doses
- **Control:** Bilateral upper arm blood pressure cuffs inflated to 50 mmHg for 4 cycles. Twice daily (am/pm) for 14 days/28 doses
- **Primary Outcome:** Death or dependency at day 90 (mRS ordinal shift analysis)



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Sites open (n=20)
Participants (n=30)

SITES & RECRUITMENT UPDATE

Open sites (20):

Site	Participants
Royal Derby Hospital	9
Queen's Medical Centre, Nottingham	2
Fairfield General Hospital, Bury	0
Aberdeen Royal Infirmary	1
UCLH	9
Morriston Hospital, Swansea	1
Bronglais General Hospital, Aberystwyth	0
Bradford Royal Infirmary	1
Southampton General Hospital	0
James Cook University Hospital, Middlesbrough	0
Salford Royal Hospital	0
Leighton Hospital, Crewe	3
Charing Cross, London	1
Leicester Royal Infirmary	1
King's College Hospital, London	1
Princess Royal University Hospital, London	0
St. George's Hospital, London	1
Royal Stoke University Hospital	0
Sunderland Royal Hospital	0
Southend University Hospital	0

Thanks to all sites for their continued support which helped us to see a great improvement in recruitment over the last month

Recruitment target: 1-2 per site per month

Please continue to send monthly screening logs to RECAST-3@nottingham.ac.uk

Sites can now view a list of other sites open to recruitment:

- Log onto the trial database
- Click on 'Data reports'
- Click on 'List of RECAST-3 hospitals'

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TRIAL UPDATES: UPCOMING AMENDMENT

Planned amendment currently in preparation:

- Change to eligibility criteria
  - NIHSS change from 5-25 to 4-25
  - Stroke onset change from ≤24 hours to ≤48 hours
- SAE reporting
  - Change from 20 days to 28 days (to accommodate treatment period that could be up to 23 days to accommodate recruitment late on day 1, missed treatments on weekends/ bank holidays)

We will keep sites updated on the progress of the amendment

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TRIAL UPDATES: EMERGENCY CONTACT NUMBERS

- We have received several emails out of hours (e.g. over the weekend) about eligibility queries.
- For any urgent queries during office hours Monday to Friday, please call the coordinating centre on 0115 8231770.
- If you aren't able to get through to the coordinating centre team to discuss your urgent query during office hours OR you have an urgent query out of hours, please use the emergency contact numbers listed on the trial website which are available when you have logged in.

REMINDER: Please also refer to the trial FAQs (currently v4.0, 17/10/2024) which may help to answer your query

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TRIAL UPDATES: CO-ENROLMENT

- Enrolment into observational studies does not require sponsor approval but please let us know those that you are taking part in.
- Co-enrolment between RECAST-3 and certain interventional trials is permitted:
  - ✓ MAPS-2
  - ✓ PhEAST
- For any other interventional trial, co-enrolment will be reviewed on a trial by trial basis and a decision taken by sponsors of both trials, with permission from the relevant safety committees. Contracts will also need to be in place.
- Record on the discharge or death in hospital CRF
- Please don’t co-enrol participants into any other trial if they have who had independent physician consent taken

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TRIAL UPDATES: OVERSEAS PATIENTS

Can overseas patients be recruited into RECAST-3?

Yes, if steps have been taken to ensure that we can collect the Day 90 follow up data.

An overseas patient can be recruited if:

i. NOK can complete follow up: Patient has a NOK in the UK who can be contacted on their behalf to provide follow up information if for example there is a language barrier or the patient doesn't have capacity. Permission to contact them directly (without prior alive and well check with GP) to be confirmed by site before recruitment. Site to also provide participant with copy of the GP letter to take home.

OR

i. Participant follow up: If no language barrier, participant has capacity and provides a phone number, site to print GP letter for participant to take home with them and ask the participant for permission to contact them directly to complete follow up rather than GP first for alive and well check.

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TRIAL UPDATES: PATIENTS DUE FOR REPATRIATION

REMINDER

For the following exclusion criteria:

'expected repatriation of the participant to another hospital not participating in RECAST-3 where RIC or sham cannot continue'

The above is applicable when it is known that a patient will be repatriated within ~72 hours. Patients that you don't expect to repatriate within the first 72 hours can be recruited if all other eligibility criteria have been met.

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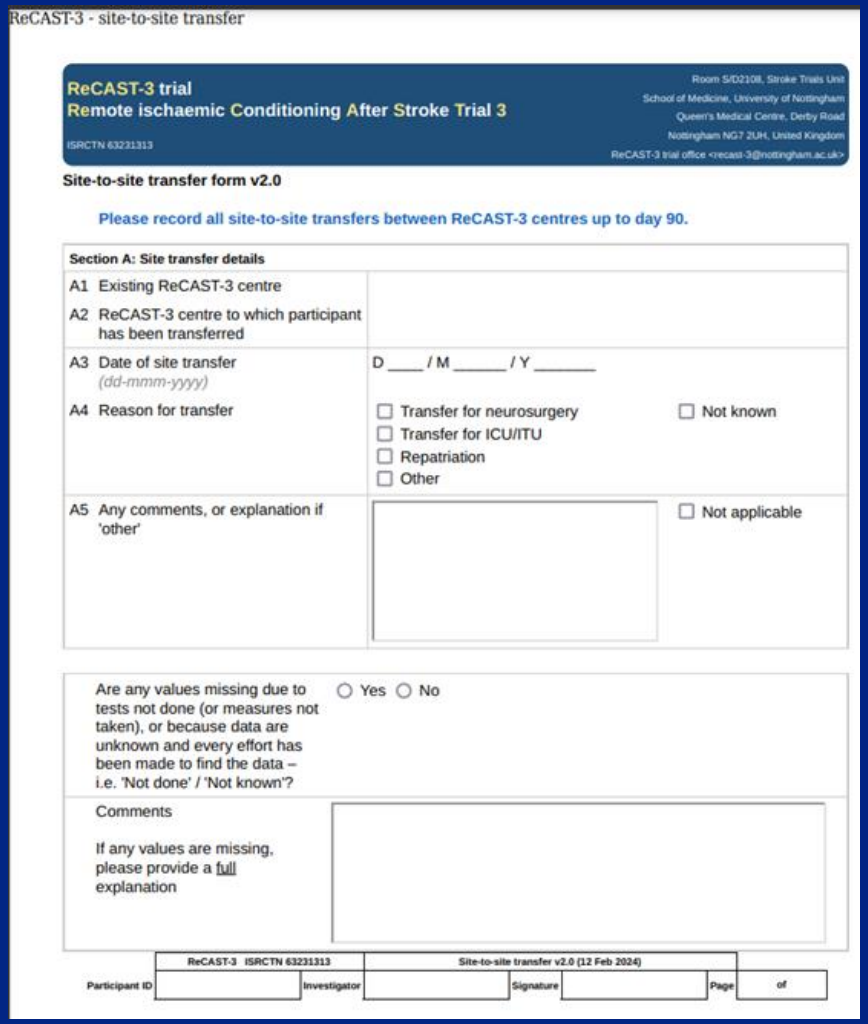
TRIAL UPDATES: SITE-TO-SITE TRANSFERS

- Please record all site-to-site transfers between RECAST-3 centres up to day 90 by completing the site-to-site transfer eCRF on the database.
- This must be to an existing RECAST-3 site.
- Once the form is submitted, an email will be automatically sent to the investigators at both sites to notify them of the transfer and confirm outstanding data that still needs to be collected. The participant will appear on the participant list for both sites.
- It is good practice to let the receiving site know that you are transferring a participant (as well as completing the eCRF). If you don't have contact details for the repat site, please let the coordinating centre know and we can contact them.



ReCAST-3 - site-to-site transfer

ReCAST-3 trial
Remote ischaemic Conditioning After Stroke Trial 3
ISRCTN 63231313

Room S/D2108, Stroke Trials Unit
School of Medicine, University of Nottingham
Queen's Medical Centre, Derby Road
Nottingham NG7 2UH, United Kingdom
ReCAST-3 trial office <recast-3@nottingham.ac.uk>

Site-to-site transfer form v2.0

Please record all site-to-site transfers between ReCAST-3 centres up to day 90.

Section A: Site transfer details

A1	Existing ReCAST-3 centre	
A2	ReCAST-3 centre to which participant has been transferred	
A3	Date of site transfer *(dd-mmm-yyyy)*	D ____ / M _____ / Y _____
A4	Reason for transfer	☐ Transfer for neurosurgery ☐ Transfer for ICU/ITU ☐ Repatriation ☐ Other ☐ Not known
A5	Any comments, or explanation if 'other'	☐ Not applicable

Are any values missing due to tests not done (or measures not taken), or because data are unknown and every effort has been made to find the data – i.e. 'Not done' / 'Not known'? ○ Yes ○ No

Comments

If any values are missing, please provide a full explanation

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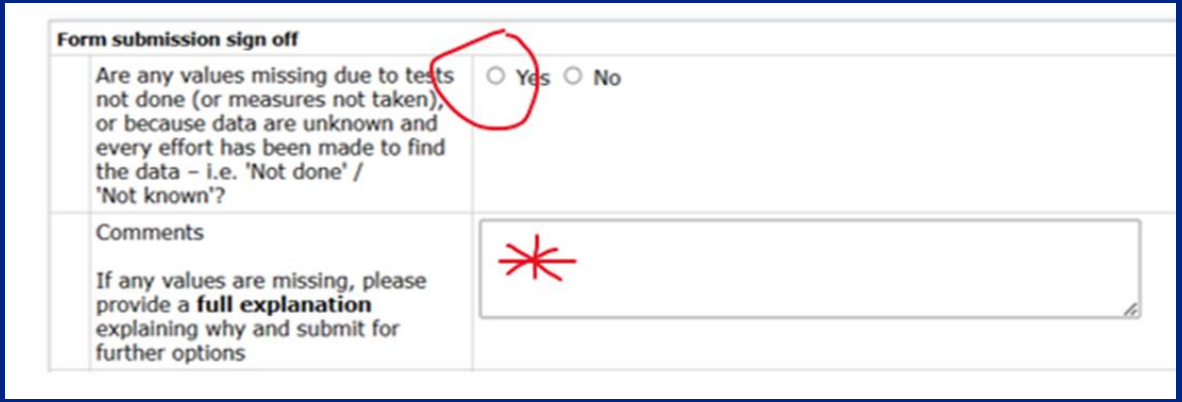
TRIAL UPDATES: ENTRY OF MISSING DATA

- **Not applicable**: measure was not required for participant
- **Not done**: if data are unavailable, either because a measure was not taken, or a test was not performed (every effort should be made to complete the test if still within the time window)
- **Not known:** if the data are unknown, and every effort has been made to find the data
- To access the hidden 'Not done' and 'Not known' options on the CRFs, please go to the bottom of the page and set the missing data control to 'Yes'. Enter a full explanation and submit the form. After this, you can complete the CRF as usual (i.e. 'Not done' and 'Not known' will be available to select



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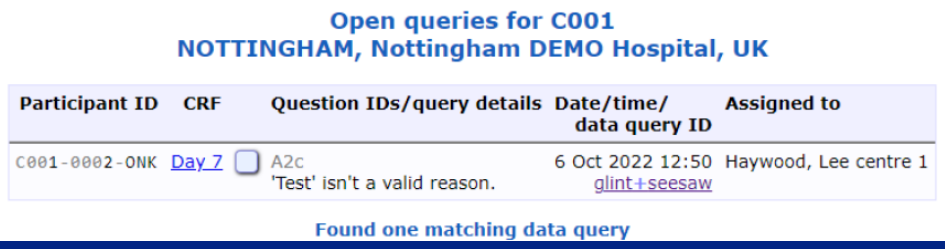
TRIAL UPDATES: DATA CORRECTIONS

The coordinating centre may raise data queries if there is missing data or if something is not quite right. Please log into the respective trial website

- TICH-3: http://tich-3.ac.uk/live/
- RECAST-3: http://recast-3.ac.uk/live/
- ENOS-2: https://stroke.nottingham.ac.uk/enos-2/live/

You will see an alert for any outstanding data queries when you click on participant list, click on this and it will show open queries for actioning.

Please click on the CRF where the data query is located i.e. in this example Day 7. You can also they can also click on the issue ID (glint+seesaw) to go directly to the specific query/questions



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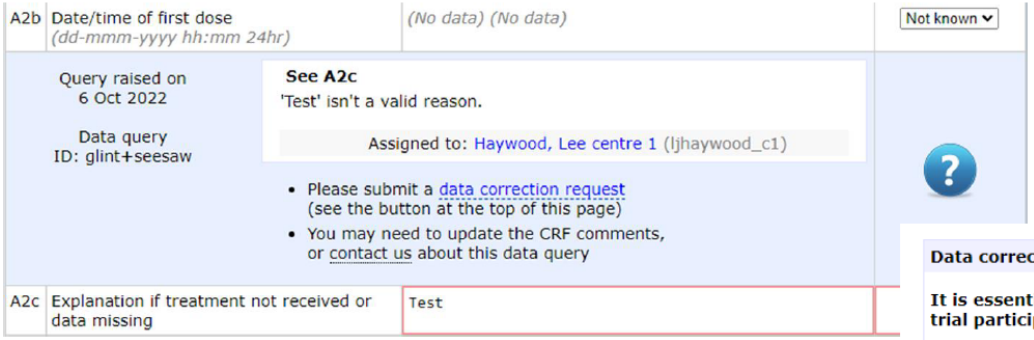
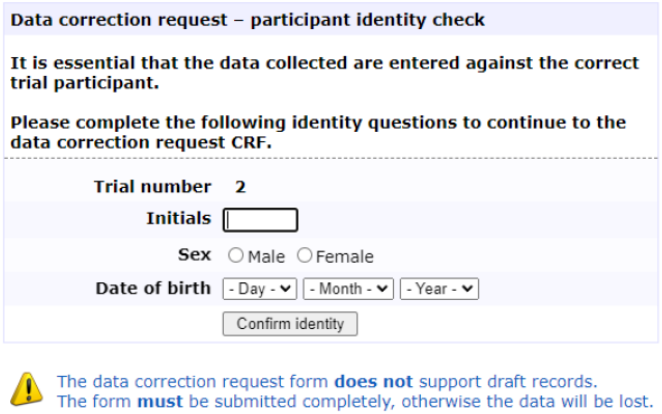
TRIAL UPDATES: DATA CORRECTIONS

The data query will show above the question where the data is to entered/amended. Please click on the link for 'data correction request'



You will then complete a participant identity check.



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TRIAL UPDATES: DATA CORRECTIONS

A5: Question ID and label is the number and title of question and the data originally entered

A6: Enter question ID of where the new data is to be entered, and the values that should appear once the CRF record has been amended

A7: Please enter the reason for the change

A5	Existing data Please list each: *Question ID* *Question label* *Data shown on report*	A2c: Explanation if treatment not received or data missing - "Test". Explanation for missing data: "Transferred before day 7".
A6	New data Please list each: *Question ID* *New value(s)*	A2c: "Participant transferred for surgery before full dose given." Explanation for missing data: "Transferred on first day for surgery".
A7	Reason for change	Required full explanation had not been given.

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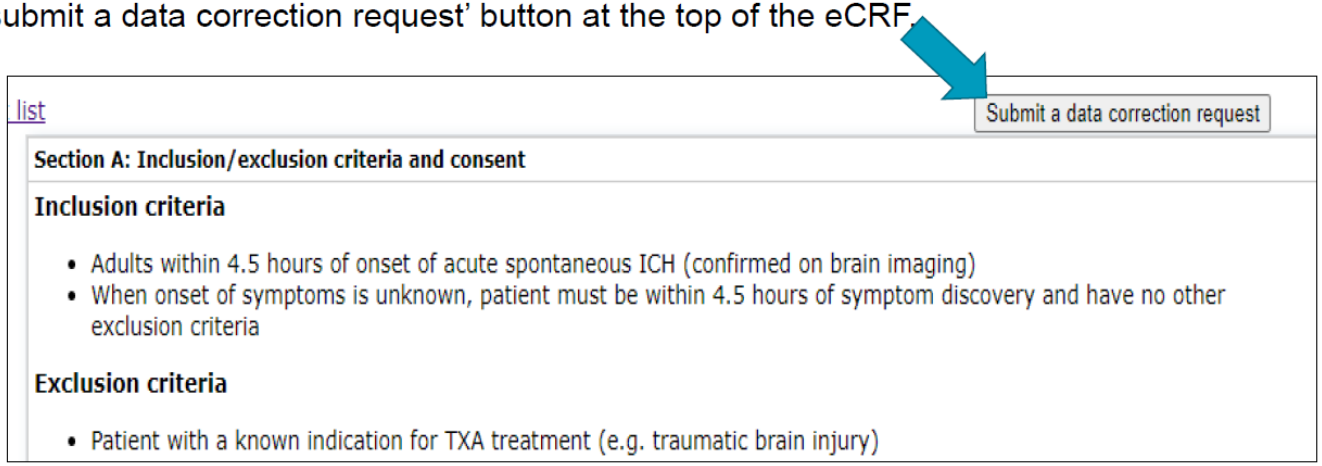
TRIAL UPDATES: DATA CORRECTIONS

You can submit a data correction request without a data query being raised by the coordinating centre e.g. if you put a comment that the EQ-5D-5L was not done at the time and would update the data later. When the data is available click on the 'submit a data correction request' button at the top of the eCRF.



As before, you will need to complete the participant identity check to access the data correction request form. If applicable, please also give existing/new text for the full explanation for missing data (state 'n/a' for 'New data' if text to be removed).

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TRIAL UPDATES: DEVICE CHECKS

- Please can we ask that sites check their AT4 tourniquet devices on a weekly basis to ensure that they are fully charged and all functions are working as required.
- For sites that haven't recruited yet or where there have been significant gaps in recruitment, please ensure that your team regularly checks that they are happy with how to use the device.
- Please notify us immediately if you notice any faults with your device or if you have any queries about the protocol.

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TRIAL UPDATES: WARD STAFF TRAINING

- We would encourage sites to involve the clinical teams where possible to assist with delivering the intervention. To do so, ward staff are required to:
- Review:
  - RECAST-3 GCP for ward staff final version 1.2 20240416.mp4
  - 995104 - Iss 01 - Product Training Guidance - AT4 Electronic Tourniquet - RECAST-3.pdf
- Optional but recommended review:
  - AT4 Device Interface controls V1.0 20240318.mp4
  - AT4 Device Participant set up and treatment delivery V1.0 20240318.mp4
  - AT4 Device Pre treatment checks V1.0 20240318.mp4
  - AT4 Device Troubleshooting V1.0 20240318.mp4
- Complete and send a copy to RECAST-3@nottingham.ac.uk:
  - RECAST-3 Ward Staff Training Log 20240419 V1.1.docx
  - RF2 TA008 Delegation Log and Codes (Ward Staff).doc

All trial documents can be found on the trial documents page

Ward staff CANNOT consent or randomise patients

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

NHS
University Hospitals of Derby and Burton
NHS Foundation Trust

End slide

Questions?

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JOINTLY FUNDED BY
UKRI Medical Research Council
NIHR National Institute for Health and Care Research

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Queries addressed during the meeting

- Overseas patients (by which we mean those who are not normally resident in the UK) can be recruited if there is someone to complete the follow up. Usually this would be a NOK who was sufficiently close to the patient to have the relevant information, but such a person must confirm their future availability and willingness at the time of recruitment.
- If a patient misses a dose completely due to undergoing other treatments, the missing dose should be made up if possible (e.g. additional dose added to the end of the treatment period). If a dose is interrupted by another treatment, practitioners should complete as much as possible, but it is not necessary to resume later. If a patient is missing doses due to not tolerating the intervention, they can be offered the opportunity to make up the missed doses, but they are not expected to do so.
- Although it is permissible to remove the cuff for the final 5-minute deflation cycle, the dose is not complete until this final 5 minutes has elapsed.
- Repatriation/discharge cannot always be predicted, and repatriation should only be used as an exclusion criterion when it is known that the patient is due to be repatriated within the first 72 hours. Otherwise, eligible patients should be recruited and receive the intervention for as long as possible up to the maximum of 14 days/28 doses.
- If a site has several active participants, capacity to deliver all doses of the intervention to all participants at the weekend may be difficult. Sites need to manage this locally and ensure that participants don't miss weekend doses unless they have received at least 4 doses post-randomisation.